

REMARKS

The Examiner noted that Applicant supplied a copy of foreign priority document RM99 A000205, but that a claim to foreign priority under 35 U.S.C. §119(a)-(d) to this document has not been made in the Oath of the Applicant. Enclosed herewith is a copy of Applicant's previously filed Supplemental Declaration in which a claim to foreign priority under 35 U.S.C. §119(a)-(d) to priority document RM99 A000205 is made. Applicant therefore respectfully requests that foreign priority to the date of this document be granted, giving due consideration to the fact that the present application is the U.S. National Stage of International Application No. PCT/IB00/00388.

Claims 1-9 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. First, with respect to claims 1, 4, 5, 6 and 9, the Examiner noted that they recite the term poloxamer. The Examiner has taken the position that poloxamer is a trade name and its use is therefore impermissible in the claims. Applicant does not agree with the Examiner that the term poloxamer is a trade name. The term poloxamer is a common name for designating a polyoxyethylene-polyoxypropylene block copolymer. Attached hereto is a copy of pertinent pages of the International Nonproprietary Names (INN) for Pharmaceutical Substances published by the World Health Organization in which it is clearly stated that a trade name for poloxamer is pluronic, evidencing that poloxamer is not a trade name but is in fact a common, or generic, name. Consequently, in view of this evidence, Applicant wishes to maintain the term poloxamer in his claims.

Separately, claims 6-9 were deemed to be indefinite as they merely recited a use without any active, positive steps illuminating how the use is actually practiced. For similar reasons

claims 6-9 have been rejected under 35 U.S.C. §101. The Examiner will please note that claims 6-9 have been cancelled and have been replaced with new claims 10-13, which claim a process for deterging contact lenses during their use. Therefore, the deficiencies noted in claims 6-9 under 35 U.S.C. §112, and 35 U.S.C. §101, are believed to have been addressed satisfactorily in new claims 10-13.

Turning now to the prior art rejections, the Examiner has rejected claims 1-4 and 6-9 as being unpatentable over WO 99/27060 in view of US-A-6 277 365.

The present invention as defined in claim 1 concerns an ophthalmic solution with viscosity enhancing and detergent properties for contact lenses, comprising hyaluronic acid or its salt with alkali or alkaline earth metals (HA) as a viscosity enhancing agent and a poloxamer as a non-ionic surfactant.

In the prior literature, it is known that the use of a surfactant, for example a poloxamer, always changes the lachrymal film leading to phenomena of intolerance.

The inventor has surprisingly found that poloxamer scarce tolerability may well be balanced by the presence of HA. This action of balance is explained as follows. It is known that the use of poloxamer leads to dry eye conditions, most probably due to the hyperevaporation of the water component of the lachrymal film, as a consequence of the alteration of its lipidic component. The alteration of such lipidic component is then counteracted by the presence of HA, which tends to entrap water on the lachrymal film, until the re-establishment of the eye physiological conditions.

The present invention, as defined in the present set of claims, has been achieved as a result of the above-unexpected findings. The formulation of the present invention allows the

prolonged use of the surfactant directly in the eye without showing any phenomena or intolerance.

The formulation of the present invention is addressing and solving the problem of an ophthalmic solution having cleaning and wetting characteristics of the contact lenses during wear with an optimal tolerability. This action is reached through a synergetic effect of two components, poloxamer and HA, where the first element exercises a cleaning action and the second tends to normalize the water component of the lachrymal film, subsequent to the alteration of the lipidic part of the poloxamer.

WO-A-99/27060 (D1) discloses, amongst a great number of aqueous solutions for cleaning, disinfecting, soaking, conditioning and wetting contact lenses, an aqueous solution which may comprise:

- a viscosity enhancing agent (for example cellulose derivatives such as HPMC); and
- a non-ionic surfactant (for example a poloxamer).

The compositions disclosed in D1 do not contain hyaluronic acid or its salt with alkali or alkaline earth metals.

In Example 5 of D1, it is suggested that a lens wearer wearing a contact lens applies one or two drops of the solution of Example 1 in the eye wearing the lens thus effecting a re-wetting of the lens and providing for comfortable and safe lens wear. However, the solution of Example 1 of D1 does not contain a poloxamer but contains a 4-(1,1,3,3-tetramethylbutyl)phenol polymer as a surfactant component.

Thus document D1 does not disclose or suggest that a composition containing a poloxamer as a surfactant and a viscosity enhancing agent may be applied directly in the eye, but only that such a composition is compatible with ocular tissue.

In summary, D1 does not disclose or suggest that a composition which contains a poloxamer is an ophthalmic composition.

In D1, the objective was to provide new contact lens treatment systems, for example multi-purpose solutions, that provide one or more benefits, for example, more effective contact lens cleaning. The problem addressed by D1 is different from the problem addressed by the present invention as defined in the amended claims.

US-B-6 277 365 (D2) discloses two different types of compositions, in particular :

- 1) an aqueous ophthalmic composition containing a quaternary nitrogen-containing ethoxylated glycoside (i.e a cationic glycoside) and an anionic therapeutic agent; and
- 2) an aqueous ophthalmic composition containing a quaternary nitrogen-containing ethoxylated glycoside (i.e a cationic glycoside) and a anionic polymer delivery vehicle in combination with a therapeutic agent.

The invention disclosed in D2 utilizes a cationic glycoside as a cationic tether, holding an anionic therapeutic agent, or an anionic delivery vehicle for a therapeutical agent, in association to the surface of the eye and or a contact lens that is worn in the eye. In the above aqueous ophthalmic solution 1), the anionic therapeutic agent may be hyaluronic acid and derivative thereof and/or salts thereof. In the above aqueous ophthalmic solution 2), hyaluronic acid and derivative thereof and/or salts thereof may be used either as the anionic delivery vehicle or as the therapeutical agent.

Thus document D2 does not disclose or suggest an ophthalmic solution with viscosity enhancing and detergent properties for contact lenses, including a poloxamer as a non-ionic surfactant.

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Further, document D2 does not disclose or suggest that hyaluronic acid or its salt with alkali or alkaline earth metals (HA) is used as a viscosity enhancing agent.

Still further, document D2 does not disclose or suggest the presence, in the ophthalmic composition, of a non-ionic surfactant as a cleaning agent for contact lenses.

The problem addressed by D2 is completely different from the problem addressed by the present invention.

As already reported above, the formulation of the present invention as defined in the claims differs mainly from the formulations as defined in D1 in that the formulation, which contains a poloxamer as a non-ionic surfactant, further contains hyaluronic acid or a salt thereof as a viscosity enhancing agent, said hyaluronuc acid allowing the prolonged use of the surfactant poloxamer directly in the eye without showing any phenomena of intolerance.

With respect to D1, the problem to solve is to replace, in a composition for treating contact lenses (*i.e cleaning, disinfecting, soaking, conditioning and wetting contact lenses*) containing a poloxamer, the viscosity inducing component (HPMC) increasing or enhancing effectiveness in removing deposit material from contact lens by an other viscosity enhancing agent in order to obtain an ophthalmic composition having cleaning and wetting characteristics of the contact lenses during wear with an optimal tolerability.

At this stage, the question to be answered is whether there is a teaching in the prior art that would prompt the skilled person, faced with the technical problem, to modify or adapt the closest prior art D1 while taking account of that teaching, thus arriving at something falling within the terms of the claims of the present invention, and thus achieving what the invention achieved. The reply is clearly no for the following reason.



As already reported above, what the invention achieves is reached through a synergetic effect of two components, poloxamer and HA, where the first element exercises a cleaning action and the second tends to normalize the water component of the lachrymal film, subsequent to the alteration of the lipidic part by the collateral action of the poloxamer, in order that the repeated usage of poloxamer in the eye does not lead not any intolerance.

D2 discloses an aqueous ophthalmic composition containing hyaluronate as an anionic therapeutical agent or as a anionic polymer vehicle.

However, the man ordinarily skilled in the art would not turn to D2 to look for guidance in modifying the D1 teachings because there is no suggestion in D1 that hyaluronic acid or its salt with alkali or alkaline earth metals would be useful to balance the scarce tolerability of a non-ionic surfactant (poloxamer) having cleaning properties on contact lenses in addition to its known advantageous properties, in particular because :

- the composition of D2 is not a cleaning solution for contact lenses;
- the composition of D2 does not contain a non-ionic surfactant; and
- the hyluronic acid in D2 must be used with a quaternary nitrogen-containing ethoxylated glycoside (i.e a cationic glycoside).

In other words, in order to solve the problem of tolerability of a non-ionic surfactant, in particular a poloxamer, a man ordinarily skilled in the art would have not been motivated to consider a document such as D2, which does not mention a non-ionic surfactant.

In Applicant's opinion, the Examiner's rejection of the claims of the present invention over D1 and D2 for obviousness is apparently the result of hindsight analysis.

In view of the above, Applicant believes that the claimed invention is unobvious over the prior art of record.

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Respectfully submitted,

By: Clifford W. Browning
Clifford W. Browning, Reg. No. 32,201
Woodard, Emhardt, Naughton,
Moriarty & McNett
Bank One Center/Tower
111 Monument Circle, Suite 3700
Indianapolis, IN 46204-5137
(317) 634-3456

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